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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/901,121	07/10/2001	Wei-Sing Chu	2313-115	8944

6449 7590 01/12/2005

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EXAMINER	
YANG, NELSON C	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 01/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/901,121	CHU, WEI-SING	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-58,61-66,68 and 69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-58,61-66,68 and 69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's amendments of claim 38 are acknowledged and have been entered.

2. Claims 38-58, 61, 64-66, 68 and 69 are pending.

Response to Arguments

Applicant's arguments, see p. 6, filed October 20, 2004, with respect to the rejection under 35 U.S.C. 112, first paragraph, have been fully considered and are persuasive. The rejection of claims 50, 52, 64, and 65 has been withdrawn.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 38 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps that delineate how ultrasound at a frequency of at least 100 kHz is used in immunohistochemistry, in situ hybridization, fluorescent in situ hybridization, Southern hybridization, Northern hybridization, Western annealing, or ELISA. Specifically, it is unclear how the ultrasound is used, when it is used, what it is directed at. It should be noted that while the claims are to be read in light of the specification, limitations in the specification may not be read into the claims.

Applicant may wish to amend the last line of the claim to "while applying ultrasound at a frequency of at least 100 kHz to the sample during deparaffinization, fixation, embedding,

rinsing, incubation, antibody localization, and hybridizing probes" in order to overcome this rejection.

With respect to claims 50, 52, applicant recites multiple transducers that produce different intensities. However, in the specification, applicant provides examples where only a single frequency such as during rinsing (p. 27, example 3, lines 18-20) and during hybridization (p. 28, example 4, lines 18-20). Furthermore, the only areas where applicant teaches the use of multiple heads and intensities is in ultrasound fixation or processing methods (p. 13-14). It is unclear whether the multiple heads and intensities are only used at these points during the assays, or if they are used throughout the entire assay, which would appear to contradict the examples provided by applicant, rendering the claims indefinite.

5. Claims 54, 55, 57 recite the limitation "said transducers" in the second line. There is insufficient antecedent basis for this limitation in the claims.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 38-40, 43, 45-48, 56, 58-64 are rejected under 35 U.S.C. 102(b) as being anticipated by Lanza et al [US, 5,958,371].

Lanza et al teaches a method of performing hybridization on a solid phase using ultrasound with a frequency of at least 100 KHz. Specifically, Lanza teaches a method of

performing hybridization (column 4, lines 43-47) on nitrocellulose membranes (column 7, lines 55-60) using ultrasound, with ultrasonic transducers suitable for biomedical and diagnostic applications within a frequency range of 5 to 50 MHz (column 7, lines 35-64).

8. With respect to claim 39, the solid phase is a tissue section. Specifically, the method is performed on a tissue surface (column 7, lines 35-40).

9. With respect to claim 40, the hybridization, annealing, or ELISA is performed on a membrane (column 7, lines 55-60).

10. With respect to claim 43, the frequency range used by Lanza et al is 5 to 50 MHz, which falls within the range of 100 KHz – 50Mhz (column 7, lines 35-64).

11. With respect to claim 45, the method is performed on a solid phase, where one or more ultrasound transducers are used to produce an ultrasound field (column 7, lines 35-64).

12. With respect to claim 46, Lanza et al teaches the use of a transducer that produces ultrasound (column 7, lines 35-64). Since the transducer head is simply the part of the transducer containing the transducer elements (see Kretz (US 4403509]), a person of ordinary skill in the art would clearly realize that the transducer Lanza et al teaches would be comprised of at least one head.

13. With respect to claim 47 and 48, Lanza et al teaches the use of a transducer that produces a broadband, or wideband, frequency (column 7, lines 55-64). Since the transducer head is simply the part of the transducer containing the transducer elements (see Kretz (US 4403509]), a person of ordinary skill in the art would clearly realize that the transducer Lanza teaches would inherently be comprised of at least one head.

14. With respect to claim 56, the method is performed on a solid phase that is rotated (column 10, example 4, column 17-18, example 10).

15. With respect to claim 58 and 60, the ultrasound is a continuous wideband frequency in the range of 0.1-50 MHz (column 7, lines 55-64).

16. With respect to claim 59, the ultrasound is a single frequency in the range of 0.1-50 MHz, specifically a 7.5 MHz focused transducer (column 9, example 3).

17. With respect to claim 61, the ultrasound is produced in pulses. Specifically, the ultrasound is operated in a pulse-echo mode (column 9-15, examples 4-7).

18. With respect to claim 62, Lanza et al teaches the use of a 7.5 MHz linear phased array transducer (columns 15-17, examples 8-9). Although Lanza et al doesn't specifically mention that the transducer produces pulses, a person of ordinary skill in the art would know that linear phased array transducers are composed of several hundred elements, with subgroups of adjacent elements producing pulses simultaneously.

19. With respect to claim 63, the ultrasound is produced as a wideband frequency in the range of 0.1-50 MHz. Specifically, the ultrasound is produced at 30-60 MHz (column 9-15, examples 4-7).

20. With respect to claim 64, the pulses vary in frequency in the range of 0.1-50 MHz (5-15 MHz) (column 14-15, example 7).

Claim Rejections - 35 USC § 103

21. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

22. Claims 38-42, 45, 48, 58, 61, 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al [Chen et al, Ultrasound-accelerated immunoassay, as exemplified by enzyme immunoassay of choriogonadotropin, 1984, Clin Chem, 30(9), 1446-1451] in view of Lee [US 6,086,821].

With respect to claim 38, Chen et al teach ultrasound accelerated ELISA methods (p.1446, col.1, pg.1) using ultrasound at frequencies of 50 kHz at 50 W. Chen et al fail to teach the use of ultrasound at frequencies above 100 kHz.

Lee, however, teaches that the forces of cavitation could destroy or rupture binding complexes indiscriminately, and can be avoided by increasing the frequency of the ultrasound optimally in the range of 80kHz – 10 MHz or by using pulsed waves (column 13, lines 50-57).

Therefore, it would have been obvious in the method of Chen et al to use ultrasound at frequencies at 80 kHz – 10 MHz, or by using pulsed waves, as suggested by Lee, in order to avoid destroying or rupturing binding complexes indiscriminately due to cavitation.

23. With respect to claims 39-42, 45, 48, 69, the antibodies can be immobilized onto filter paper or microtiter-plates (p.1447, col.2, pg. 3). Test strips containing ~0.3 cm^2 of immobilized antibody paper were also used (p.1447, col.2, pg.6) with ultrasound with a nominal acoustic power of 50 W (p.1447, col.2, pg.2). With respect to claim 43, Lee teach the use of ultrasound of a frequency in the range of 80kHz – 10MHz (column 13, lines 50-57).

24. With respect to claims 58, 66, the test strips were sonicated for 20 min. before incubation (p.1449, col.2, pg. 1).

25. With respect to claim 61, Lee teaches the use of pulsed waves (column 13, lines 50-57) with pulses of less than 20 msec (column 14, lines 1-2).

26. Claims 41, 42, and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lanza et al [US 5,958,371] in view of Gravlee, Jr [US 3,961,097].

The method of Lanza et al as disclosed above fails to recite the specific feature of ultrasound receiving power in the range of 0.01-100 W/cm^2. However, Gravlee, Jr. teaches that the intensity of ultrasound must be maintained at a level below the level at which damage to cells in the tissue occurs. It would have been obvious for a person of ordinary skill in the art to use an ultrasound receiving power within this particular range in order to avoid damaging the sample, because it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. At 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since applicant has not disclosed that the specific limitations recited in instant claims 41, 42, and 69 are for any particular purpose or solve any stated problem and the prior art teaches that improved noninvasive method for forming an acoustic contrast agent which can be targeted in vitro or in vivo and which when bound to a specific desired site alters the acoustic reflectivity of a tissue surface or support media in a manner detectable using ultrasonic transducers, absent

unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by Lanza et al by normal optimization procedures known in the art in order to avoid damaging the sample.

27. Claims 44, 51, 53-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lanza et al [US 5,958,371], in view of Blank [US 5,913,826] and Lang et al [US 5,941,825].

a. Lanza et al teaches a method involving the use of transducers to produce ultrasound (column 7, lines 35-64). Lanza et al does not specifically teach the use of two or more transducers to produce ultrasound.

28. Blank, however, teaches the use of a multiple transducer array in order to fit a three-dimensional contour (column 13, lines 19-29). Lang et al further teaches that the ultrasound system can contain three ultrasound sources transmitting at three different frequencies and separated by predetermined distances. Detection of returning signals can include sampling of all the returning frequencies at all detector sites, which effectively allows each ultrasound source to be coded and the returning signals can be identified with a particular ultrasound source. This permits greater refinement of reflective distances because the reflective distance from each ultrasound source is separately detected at each detector, which facilitates signal averaging and can optionally provide a basis of triangulation between different ultrasound sources and the reflective interfaces in order to verify reflective distances. This essentially permits detection from multiple reflective angles (column 24, lines 1-20). Therefore it would be obvious to use two or more transducers in the method disclosed by Lanza et al, in order to fit a three-dimensional contour or to permit detection from multiple reflective angles.

29. With respect to claim 51, although Lanza et al does not teach the step of having each transducer produce a different frequency, Lang et al teaches that ultrasound sources transmitting at different frequencies permits greater refinement of reflective distances because the reflective distance from each ultrasound source is separately detected at each detector, which facilitates signal averaging and can optionally provide a basis of triangulation between different ultrasound sources and the reflective interfaces in order to verify reflective distances (column 24, lines 1-20). Therefore, it would be obvious to produce different ultrasound frequencies in the method of Lanza et al, in order to permit detection from multiple reflective angles.

30. With respect to claim 53, Lanza et al teaches the application of a range of frequencies to a sample (column 14-15, example 7).

31. With respect to claim 54, Lanza et al discloses a method where the transducers are arranged in a two-dimensional arrangement (columns 9-17, examples 4-9)

32. With respect to claim 55, although Lanza et al does not disclose a method where the transducers are arranged in a three-dimensional arrangement, Blank teaches it would be obvious to use multiple transducers in order to fit a three-dimensional contour. Therefore, it would be obvious to use multiple transducers arranged in a three-dimensional arrangement in the method disclosed by Lanza in order to fit a three-dimensional contour.

33. Claims 46-49, and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lanza et al [US 5,958,371], in view of Kretz [US 4,403,509].

While Lanza et al teaches the use of a transducer comprising of a head to produce ultrasound, he does not teach the use of a transducer with multiple heads (column 7, lines 35-64). Kretz, however, teaches that the use of multiple transducer heads will allow the entire image to

have a higher resolution. (column 3, lines 7-30). Therefore it would be obvious to use a transducer with multiple heads in the method disclosed by Lanza et al, in order to achieve an image with higher resolution.

34. With respect to claims 47 and 48, Lanza et al teaches the use of transducers capable of emitting wideband frequency (columns 9-17, examples 4-9).

35. With respect to claim 49, although Lanza et al does not teach the use of multiple heads producing different frequencies, Kretz teaches that sound at different frequencies may be used for an examination at different depths. Particularly, regions near the surface may be examined with sound at higher frequencies than regions at larger depths. Higher sound frequencies will inherently involve a higher resolution and will also involve a lower depth of penetration into the object, which may consist of organic tissue. That lower depth of penetration may be desirable in such case as it will help to avoid ghost echoes (column 3, lines 21-47). Therefore it would be obvious to use a transducer comprising of multiple heads producing different frequencies in the method of Lanza et al, in order to allow for examination at different depths, and to avoid ghost echos.

36. With respect to claim 57, although Lanza et al teaches the use of a solid phase and a transducer (column 7, lines 35-64), he does not teach that the step of rotating the transducer around the solid phase. Kretz, however, teaches that if the wheel is rotated at constant speed and each group consists of the same number of sound transducer heads, the sound transducer heads of the group designed in accordance with the invention may be used to produce section images having a high lateral resolution. Therefore, it would be obvious to rotate the transducer in the method of Lanza et al, in order to produce section images having a high lateral resolution.

Response to Arguments

37. Applicant's arguments filed October 20, 2004, with respect to the rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103(a) have been fully considered but they are not persuasive. Applicant argues that Lanza describes ultrasound-based ELISA-type laboratory diagnostic assays and not an ELISA itself, such that Lanza is concerned with ultrasonic imaging and not with the ELISA itself.

38. This is not found persuasive for the reason that the detection step in an assay is not separate from the assay itself, and therefore Enzyme-linked immunosorbent assays would contain a detection step, in the case of Lanza, one involving ultrasound.

It should be noted that it is acknowledged and agreed with that the ultrasound taught by Lanza is used for an entirely different purpose than that taught by applicant according to applicant's disclosure. However, since applicant has merely recited the use of ultrasound at a frequency of at least 100 kHz in claim 38, this limitation would read upon the prior art, as it does not specify how the ultrasound is to be used in immunohistochemistry, in situ hybridization, Southern hybridization, Northern hybridization, Western annealing, and ELISA, whether it is for diagnostic purposes such as in Lanza, for lysing purposes, for mixing purposes, or some other unknown purpose not specified by applicant.

It should be noted that while the claims are to be read in light of the specification, limitations in the specification **may not** be read into the claims.

For these reasons, the rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103(a) have been maintained.

Conclusion

39. No claims are allowed.

40. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

41. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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